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FEE TRANSMITTAL
For FY 2005

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 500

Complete if Known	
Application Number	10/691113
Filing Date	22 October 2003
First Named Inventor	Boris Shekunov
Examiner Name	Joseph W. Drodge
Art Unit	1723
Attorney Docket No.	FER-14651

METHOD OF PAYMENT (check all that apply)

☐ Check ☐ Credit Card ☐ Money Order ☐ None ☐ Other (please identify): ____

☑ Deposit Account Deposit Account Number: 060625 Deposit Account Name: Ferro Corporation

For the above-identified deposit account, the Director is hereby authorized to: (check all that apply)

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FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES

	FILING FEES		SEARCH FEES		EXAMINATION FEES		
Application Type	**Fee ($)**	**Small Entity Fee ($)**	**Fee ($)**	**Small Entity Fee ($)**	**Fee ($)**	**Small Entity Fee ($)**	**Fees Paid ($)**
Utility	300	150	500	250	200	100	
Design	200	100	100	50	130	65	
Plant	200	100	300	150	160	80	
Reissue	300	150	500	250	600	300	
Provisional	200	100	0	0	0	0	

2. EXCESS CLAIM FEES

Fee Description	**Fee ($)**	**Small Entity Fee ($)**
Each claim over 20 or, for Reissues, each claim over 20 and more than in the original patent	50	25
Each independent claim over 3 or, for Reissues, each independent claim more than in the original patent	200	100
Multiple dependent claims	360	180

Total Claims ____ - 20 or HP = **Extra Claims** ____ x **Fee ($)** ____ = **Fee Paid ($)** ____

HP = highest number of total claims paid for, if greater than 20

Indep. Claims ____ - 3 or HP = **Extra Claims** ____ x **Fee ($)** ____ = **Fee Paid ($)** ____

HP = highest number of independent claims paid for, if greater than 3

Multiple Dependent Claims

Fee ($) 0 **Fee Paid ($)** 0

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper, the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets ____ - 100 = **Extra Sheets** ____ / 50 = **Number of each additional 50 or fraction thereof** ____ (round **up** to a whole number) x **Fee ($)** ____ = **Fee Paid ($)** ____

4. OTHER FEE(S) **Fees Paid ($)**

Non-English Specification, $130 fee (no small entity discount) ____

Other: Appeal Brief 500

SUBMITTED BY

Signature	[signature]	Registration No. (Attorney/Agent) 32,119	Telephone 216-566-9700
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8 April 2005
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Kathryn A. Kallay
Signature of Person Mailing Paper

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	10/691,113
Cnfrm. No.	:	5325
First Named Inventor	:	Boris Y. Shekunov
Filed	:	October 22, 2003
Title	:	METHOD AND APPARATUS FOR PRODUCING PARTICLES VIA SUPERCRITICAL FLUID PROCESSING
TC/A.U.	:	1723
Examiner	:	Joseph W. Drodge
Docket No.	:	FER-14651

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APPEAL BRIEF

Sir:

This Appeal Brief is being filed in accordance with 37 C.F.R. §41.37 within two months of the Notice of Appeal that was filed in this matter on February 11, 2005.

I. REAL PARTY IN INTEREST

The real party in interest or owner of the present application and the technology and inventions embodied therein is The Ferro Corporation, an Ohio Corporation, whose principal place of business is 1000 Lakeside Avenue, Cleveland, Ohio 44114. An assignment transferring rights from the inventors to The Ferro Corporation was recorded February 19, 2004 at Reel 014994, Frame 0915.

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II. RELATED APPEALS AND INTERFERENCES

The application is not involved in an interference proceeding and there are no related appeals.

III. STATUS OF CLAIMS

The application was filed on October 22, 2003 with twenty (20) original claims. In a first Office Action mailed on July 30, 2004 (Paper No./Mail Date 0704), the Examiner rejected claims 1-20. On October 25, 2004, applicants filed an Amendment that amended claim 16, canceled claim 20 and addied new claims 21-37 to the application. In a second Office Action mailed on November 12, 2004 (Paper No./Mail Date 1104), the Examiner finally rejected all pending claims (i.e., claims 1-19 and 21-37) under 35 U.S.C. §102(e). On February 11, 2005, applicants filed a Notice of Appeal from the final rejection of claims 1-19 and 21-37. The pending claims are set forth in the Claims Appendix, which is attached hereto for the convenience of the Board.

IV. STATUS OF AMENDMENTS

No amendments were filed in the application subsequent to the final rejection mailed November 12, 2004 (Paper No./Mail Date 1104).

V. SUMMARY OF CLAIMED SUBJECT MATTER

As noted in paragraphs [0015-0016] of the application, the present invention provides a method of producing particles using an enhanced mixing technique. In accordance with the claimed method, a supercritical fluid is continuously flowed through a mixing chamber that has a rotating rotor disposed therein. A solution that comprises a solute dissolved or dispersed in a solvent that is at least partially soluble in the supercritical fluid is dispensed into a mixing zone, which is defined as a space between an inner wall of the chamber and an adjacent surface of the rotating rotor disposed within the chamber. The solution rapidly mixes with the supercritical fluid in the mixing zone as a result of high shear forces, centrifugal forces and turbulence created between the spinning rotor surface and the inner wall of the chamber, which causes the solvent to rapidly dissolve from the solution into the supercritical fluid, thus forming a mixture of solvent and supercritical fluid [see paragraphs 0047-0048]. The loss of solvent from the solution results in supersaturation, which causes the solute to precipitate into the mixture of solvent and supercritical fluid in the form of small particles [0048]. In a second embodiment of the invention,

a second solution is simultaneously dispensed into the mixing zone together with the first solution to produce particles that comprise a first and second solute, which may have a core-shell configuration [0060]. The precipitated particles are recovered from the mixture of supercritical fluid and solvent via filtration [0050]. The method is particularly useful for producing biologically active medicinal substances [0052]. The claimed methods allow for the controlled production of particles having a more uniform morphology and/or size than is achievable using conventional particle production methods.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Whether claims 1-19 and 21-37 were properly rejected under 35 U.S.C. §102(e) as being anticipated by Johnson et al., U.S. Pat. App. Pub. No. US2004/0091546 A1.

VII. ARGUMENT

Claims 1-19 And 21-37 Were Improperly Rejected Under 35 U.S.C. §102(e)

A. *Claims 1-5, 7, 8, 10-13 and 15-19 (Grouped)*

Claim 1 claims:

> A method of producing particles comprising the steps of:
> providing a supercritical fluid;
> providing a first solution, the first solution comprising a first solute dissolved or dispersed in a first solvent that is at least partially soluble in the supercritical fluid;
> flowing the supercritical fluid through a chamber having a rotating rotor disposed therein;
> dispensing the first solution into a mixing zone within the chamber while the supercritical fluid is flowing through the chamber, the mixing zone being defined as a space between an inner wall of the chamber and an adjacent surface of the rotating rotor; and
> collecting precipitated particles of the first solute from a mixture comprising the supercritical fluid and the first solvent.

The Examiner rejected claim 1 under 35 U.S.C. §102(e) as being anticipated by Johnson et al., U.S. Pat. App. Pub. No. US2004/0091546 A1 (hereinafter "Johnson et al."). This rejection is clearly improper because each and every element as set forth in claim 1 cannot be found, either expressly or inherently, in Johnson et al. See *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Johnson et al. disclose a process for forming nanoparticles of amphiphilic copolymers, which are copolymers comprised of subunits or monomers that have different hydrophilic and hydrophobic characteristics (see page 5, paragraph [0050]). In accordance with the method disclosed in Johnson et al., an amphiphilic copolymer is dissolved in a process solvent (see page 2, paragraph [0018]). The process solvent comprising the amphiphilic copolymer is then rapidly mixed with a non-process solvent that is capable of changing the charge of the local molecular environment of the amphiphilic copolymers (see page 2, paragraph [0011]). Johnson et al. teach that the mixing of the process solvent with the non-process solvent can be achieved using either a continuous flash mixer or a batch flash mixer (see page 2, paragraph [0015]).

A continuous flash mixer is schematically illustrated in FIG. 1 of Johnson et al., which shows two inlets (one inlet for the process solvent and one inlet for the non-process solvent) to a conical-domed mixing vessel with a conical outlet. The schematically illustrated continuous flash mixer shown in FIG. 1 does not include a rotating rotor, but Johnson et al. do mention on page 4 in paragraph [0041] that the mixing vessel could be a rotor stator mixer, where the process solvent is introduced into the region of high mixing velocity. No further explanation of the configuration of a continuous flash mixer comprising a rotor stator is given.

A batch flash mixer is schematically illustrated in FIG. 2, which shows an inlet tube positioned proximate to a mixing or agitating device such as a rotor disposed in a mixing vessel. Johnson et al. mention on page 4 in paragraph [0043] that the process solvent containing the amphiphilic copolymer is added via the inlet tube to the non-process solvent in the mixing vessel into a region of high mixing intensity, near the sweep region of the mechanical agitator (see page 4, paragraph [0044]). While the batch flash mixer of Johnson et al. does contain a rotating mechanical agitator or rotor disposed in a mixing vessel, the non-process solvent does not flow through the mixing vessel as required by the claimed method.

Johnson et al. teach that the non-process solvent must be capable of changing the local molecular environment of the amphiphilic copolymer and cause local precipitation of either the hydrophobic or hydrophilic blocks (see page 7, paragraph [0063]). Johnson et al. teach that the non-process solvent can be water or an aqueous solution containing a buffering agent, salt, colloid dispersant, or inert molecule, or could be a mixture of solvents such as alcohol and water (see page 7, paragraph [0063]). On page 6, at paragraph [0058], Johnson et al. teach that:

> "In another embodiment of the invention, the process or non-process solvent may consist of a liquefied gas. In this embodiment, the process or non-process

> solvents are a gas at room temperature but are put in liquid form for the process by changing the pressure or temperature or both in the mixing vessel or inlet tubes. An example of a liquefied gas used as a non-process solvent is carbon dioxide under adequate pressure with or without a modifier, such as ethanol. After mixing, a post processing step consisting of a pressure or temperature change or a change in both is made and the solvent evaporates leaving the nanoparticles."

The Examiner contends that in the above-quoted paragraph, Johnson et al. teach that the non-process solvent (referred to as an "antisolvent" by the Examiner) may be supercritical carbon dioxide. Applicants respectfully disagree. In the above-quoted paragraph, Johnson et al. teach that <u>liquid</u> carbon dioxide may be used as a process solvent or a non-process solvent, but liquid carbon dioxide is not the same as <u>supercritical</u> carbon dioxide. Carbon dioxide can only exist in a supercritical state at a pressure greater than 1,070 pounds per square inch (psi) and a temperature greater than 31°C. Johnson et al. do not specify that supercritical fluid should be used in the process.

The Examiner also refers to page 7, paragraph [0063] of Johnson et al. as supporting his contention that supercritical carbon dioxide is contemplated for use as a non-process solvent. Applicants respectfully submit that the Examiner is in error. At page 7, paragraph [0063], Johnson et al. teach in pertinent part that:

> "The final solvent containing the nanoparticles (sic) can be altered by a number of post treatment processes, such as but not limited to dialysis, distillation, wiped film evaporation, centrifugation, lyophilization, filtration, sterile filtration, extraction, supercritical fluid extraction, or spray drying. The processes typically occur after the nanoparticle formation but could also occur during the nanoparticle formation process."

The teachings set forth in paragraph [0063] very clearly relate to "post treatment processes" for altering the "final solvent containing the nanoparticles". Each of the processes mentioned by Johnson et al. is a process that can be used to separate the already-formed nanoparticles from the resulting <u>final</u> solvent. These processes are not alternative embodiments of the basic invention disclosed by Johnson et al., which results in the production of a "final solvent containing the nanoparticles". Thus, Johnson et al. clearly mention "supercritical fluid extraction" only in the context of being one of the post treatment processes that can be used to alter the final solvent containing the nanoparticles.

Johnson et al. clearly know the difference between liquid carbon dioxide and supercritical carbon dioxide. They mention liquid carbon dioxide as a potential process or non-process solvent, and supercritical fluid extraction as a potential post treatment process. But they do not teach, suggest or disclose supercritical carbon dioxide or any other supercritical fluids as potential non-process solvents as required by claim 1.

Applicants further note that Johnson et al. does not teach or suggest "dispensing the first solution into a mixing zone within the chamber while the supercritical fluid is flowing through the chamber, the mixing zone being defined as a space between an inner wall of the chamber and an adjacent surface of the rotating rotor" as required by claim 1. As previously noted, Johnson et al. teach the use of either of two types of flash mixers: a continuous flash mixer or a batch flash mixer. A batch flash mixer includes a rotating rotor disposed in a chamber, but no supercritical fluid is flowed through the chamber as required by claim 1. A non-process solvent is flowed through a chamber of a continuous flash mixer, which can include a rotor stator, but Johnson et al. do not teach dispensing the process solvent "into a mixing zone [...] defined as a space between an inner wall of the chamber and an adjacent surface of a rotating rotor" as required by claim 1. The continuous flash mixer illustrated in FIG. 1 of Johnson et al. does not depict any rotating rotor, and thus does not depict dispensing the process solvent into a mixing zone between an inner wall of the chamber and an adjacent surface of a rotating rotor. This element of claim 1 is completely missing from Johnson et al. Therefore, Johnson et al. clearly does not anticipate claim 1.

Claims 2-5, 7, 8, 10-13 and 15-19 depend from claim 1 either directly, or through an intervening claim. Thus, claims 2-5, 7, 8, 10-13 and 15-19 include all of the limitations set forth in claim 1, and are not anticipated by Johnson et al. for the same reasons that claim 1 is not anticipated by Johnson et al.

B. *Claim 6*

Claim 6 depends from claim 1 and further specifies that "the inner wall of the chamber is spaced apart from the surface of the rotating rotor a distance of from about 0.1 mm to about 2.5 mm". As noted above, Johnson et al. mention that a continuous flash mixer that includes a rotor stator can be used, but they do not provide any information regarding the configuration of such a mixer. Johnson et al. describe continuous flash mixers on page 4, paragraphs [0037-0041], but never suggest dispensing the process solvent into a mixing zone "defined as a space

between an inner wall of the chamber and an adjacent surface of the rotating rotor", where the "the inner wall of the chamber is spaced apart from the surface of the rotating rotor a distance of from about 0.1 mm to about 2.5 mm" as required by claim 6. Clearly, Johnson et al. does not anticipate claim 6.

C. *Claim 9*

Claim 9 depends from claim 8, which depends from claim 7, which depends from claim 1. Claim 9 specifies that a first solution is dispensed into the mixing zone of the mixing chamber through a first solution port, a second solution is dispensed into the mixing zone of the mixing chamber through a second solution port, and "the first solution port and the second solution port are coaxial". Johnson et al. does not eve teach, suggest or disclose dispensing two process solvents into a mixing zone through coaxial ports. Johnson et al., therefore, does not anticipate claim 9.

D. *Claim 14*

Claim 14 depends from claim 1 and specifies that that the first solution comprises an emulsion. Johnson et al. does not teach or suggest that the process solvent comprising the amphiphilic copolymer could be an emulsion. The word "emulsion" appears only one time in Johnson et al., and that is on page 9, paragraph [0077], wherein Johnson et al. teach that the particles produced by a flash precipitation according to the invention can be formulated into a pharmaceutically acceptable liquid dosage form for oral administration such as an emulsion. Claim 14, therefore, is not anticipated by Johnson et al.

E. *Claims 21-37 (Grouped)*

Claim 21 is an independent claim directed to the second embodiment of the invention disclosed in paragraphs [0054-0060] of the application. Claims 22-37 depend from claim 21 and thus include all of the limitations set forth in claim 21. Claim 21 includes all of the limitations of claim 1 that make claim 1 patentable over Johnson et al. Claim 21 claims (*italicized* emphasis added):

> A method of producing particles comprising the steps of:
> providing a supercritical fluid;
> providing a first solution, the first solution comprising a first solute

dissolved or dispersed in a first solvent that is at least partially soluble in the supercritical fluid;
providing a second solution, the second solution comprising a second solute dissolved or dispersed in a second solvent that is at least partially soluble in the supercritical fluid;
flowing the supercritical fluid through a chamber having a rotating rotor disposed therein;
dispensing the first solution through a first solution port into a first portion of a mixing zone within the chamber while the supercritical fluid is flowing through the chamber, the mixing zone being defined as a space between an inner wall of the chamber and an adjacent surface of the rotating rotor;
dispensing the second solution through a second solution port into a second portion of the mixing zone at the same time the first solution is being dispensed into the mixing zone;
precipitating particles into a mixture comprising the supercritical fluid, the first solvent and the second solvent, the *precipitated particles having a core structure comprising the first solute and a shell structure comprising the second solute*; and
collecting the precipitated particles from the mixture.

The Examiner contends in the last line on the bottom of page 2 of the Office Action of November 12, 2004 (Paper No./Mail Date 1104) that "forming coated cores is disclosed at para 34" of Johnson et al. On page 3, at paragraph [0034], Johnson et al. teach that (emphasis added):

> The present invention relates to a process and apparatuses preparing nanoparticles from amphiphilic copolymers,. The size of the resulting nanoparticles can be controlled by controlling the mixing velocity used to create them. Nanoparticles can be produced from amphiphilic copolymers that are dissolved in a process solvent. After the amphiphilic copolymers are dissolved in the process solvent, the solution is rapidly mixed with a non-process solvent and nanoparticles are flash precipitated in the resulting solution. This mixing can be achieved through various methods during which the mixing velocity is controlled. In addition, *an additive target molecule can be mixed with the amphiphilic copolymer in the process solvent prior to flash precipitation for incorporation into the resulting nanoparticles.*

Applicants agree that Johnson et al. disclose forming coated additive target molecules that could have a core-shell configuration, but applicants contend that the manner in which Johnson et al. teach the formation of such coated additive target molecules does not anticipate claims 16 and 21-37. In the process disclosed in Johnson et al., the additive target molecule is mixed with the amphiphilic copolymer in the process solvent prior to flash precipitation.

Johnson et al. do not teach that the additive target molecule and the amphiphilic copolymer should be added into a mixing zone as separate solution streams as claimed. On page 6, at paragraphs [0057] to page 7, at paragraph [0063], Johnson et al. further discuss incorporation of additive target molecules in the particles. In each case, the additive target molecules are introduced with the amphiphilic copolymer in the process solvent, and not as a separate stream from a second solution. Applicants respectfully submit that Johnson et al. does not disclose, teach or suggest precipitating particles having a core-shell structure, where the core comprises a first solute and the shell comprises the second solute and the solutes are introduced into the mixing zone as separate solutions. Claims 16 and 21-37 are clearly not anticipated by Johnson et al.

Conclusion

In view of the foregoing, it is respectfully submitted that claims 1-19 and 21-37 are allowable over the prior art references of record, and a ruling from the Board to that effect is therefore respectfully requested.

Respectfully submitted,

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CLAIMS APPENDIX

Claim 1 (original): A method of producing particles comprising the steps of:

providing a supercritical fluid;

providing a first solution, the first solution comprising a first solute dissolved or dispersed in a first solvent that is at least partially soluble in the supercritical fluid;

flowing the supercritical fluid through a chamber having a rotating rotor disposed therein;

dispensing the first solution into a mixing zone within the chamber while the supercritical fluid is flowing through the chamber, the mixing zone being defined as a space between an inner wall of the chamber and an adjacent surface of the rotating rotor; and

collecting precipitated particles of the first solute from a mixture comprising the supercritical fluid and the first solvent.

Claim 2 (original): The method of producing particles according to claim 1 wherein the rotating rotor intimately mixes the first solution and the supercritical fluid together via shear mixing, turbulent mixing and/or centrifugal mixing.

Claim 3 (original): The method of producing particles according to claim 1 wherein the first solution is dispensed into the mixing zone through one or a plurality of ports provided in the inner wall of the chamber.

Claim 4 (original): The method of producing particles according to claim 1 wherein the rotating rotor is a smooth drum, a grooved drum, a propeller rotor or a turbine rotor.

Claim 5 (original): The method of producing particles according to claim 1 wherein the rotor rotates within the chamber at a speed of from about 100 to about 20,000 RPM when the solution is being dispensed into the mixing zone.

Claim 6 (original): The method of producing particles according to claim 1 wherein the inner wall of the chamber is spaced apart from the surface of the rotating rotor a distance of from about 0.1 mm to about 2.5 mm.

Claim 7 (original): The method of producing particles according to claim 1 further comprising the steps of:

providing a second solution, the second solution comprising a second solute dissolved or dispersed in a second solvent that is at least partially soluble in the supercritical fluid; and

dispensing the second solution into the mixing zone at the same time the first solution is being dispensed into the mixing zone.

Claim 8 (original): The method of producing particles according to claim 7 wherein the first solution is dispensed into the mixing chamber through a first solution port and the second solution is dispensed into the mixing chamber through a second solution port.

Claim 9 (original): The method or producing particles according to claim 8 wherein the first solution port and the second solution port are coaxial.

Claim 10 (original): The method of producing particles according to claim 8 wherein the first solution port and the second solution port are formed in the inner wall of the chamber at different locations within the mixing zone.

Claim 11 (original): The method according to claim 7 wherein the first solvent and the second solvent are the same.

Claim 12 (original): The method according to claim 1 wherein the first solute is selected from the group consisting of biologically active materials, medicinal agents, sugars, pigments, toxins, insecticides, viral materials, diagnostic aids, agricultural chemicals, nutritional materials, proteins, alkyloids, alkaloids, peptides, animal and/or plant extracts, dyes, explosives, paints, polymer precursors, cosmetics, antigens, enzymes, catalysts, nucleic acids, and combinations thereof.

Claim 13 (original): The method according to claim 1 wherein the supercritical fluid is carbon dioxide.

Claim 14 (original): The method according to claim 1 wherein the first solution comprises an emulsion.

Claim 15 (original): The method according to claim 1 wherein the first solution comprises a suspension of the first solute in the form of solid phase particles dispersed in the first solvent.

Claim 16 (previously presented): The method according to claim 15 wherein a polymer, lipid and/or excipient is dissolved in the second solvent, and the precipitated particles collected in the collecting step have a core comprising the first solute and a shell comprising the polymer, lipid and/or excipient.

Claim 17 (original): The method according to claim 1 wherein the particles collected in the collecting step are substantially uniform and have an average diameter of less than about 5 μm.

Claim 18 (original): The method according to claim 1 further comprising the step of: adjusting the rotational speed of the rotor, the size of the space between the inner surface of the chamber and the adjacent surface of the rotor, and/or the flow rate of the supercritical fluid and/or first solution into the chamber to obtain precipitated solute particles having a desired average particle size.

Claim 19 (original): Particles formed according to the method of claim 1.

Claim 20 (canceled)

Claim 21 (previously presented): A method of producing particles comprising the steps of:

providing a supercritical fluid;

providing a first solution, the first solution comprising a first solute dissolved or dispersed in a first solvent that is at least partially soluble in the supercritical fluid;

providing a second solution, the second solution comprising a second solute dissolved

or dispersed in a second solvent that is at least partially soluble in the supercritical fluid;

flowing the supercritical fluid through a chamber having a rotating rotor disposed therein;

dispensing the first solution through a first solution port into a first portion of a mixing zone within the chamber while the supercritical fluid is flowing through the chamber, the mixing zone being defined as a space between an inner wall of the chamber and an adjacent surface of the rotating rotor;

dispensing the second solution through a second solution port into a second portion of the mixing zone at the same time the first solution is being dispensed into the mixing zone;

precipitating particles into a mixture comprising the supercritical fluid, the first solvent and the second solvent, the precipitated particles having a core structure comprising the first solute and a shell structure comprising the second solute; and

collecting the precipitated particles from the mixture.

Claim 22 (previously presented): The method of producing particles according to claim 21 wherein the rotating rotor intimately mixes the first solution and the supercritical fluid together via shear mixing, turbulent mixing and/or centrifugal mixing.

Claim 23 (previously presented): The method of producing particles according to claim 21 wherein the first solution is dispensed into the mixing zone through a plurality of first solution ports into the chamber.

Claim 24 (previously presented): The method of producing particles according to claim 21 wherein the rotating rotor is a smooth drum, a grooved drum, a propeller rotor or a turbine rotor.

Claim 25 (previously presented): The method of producing particles according to claim 21 wherein the rotor rotates within the chamber at a speed of from about 100 to about 20,000 RPM when the first solution and the second solution are being dispensed into the mixing zone.

Claim 26 (previously presented): The method of producing particles according to claim 21 wherein the inner wall of the chamber is spaced apart from the surface of the rotating rotor a distance of from about 0.1 mm to about 2.5 mm.

Claims 27 (previously presented): The method or producing particles according to claim 21 wherein the first solution port and the second solution port are coaxial.

Claim 28 (previously presented): The method of producing particles according to claim 21 wherein the first solution port and the second solution port are formed in the inner wall of the chamber at different locations within the mixing zone.

Claim 29 (previously presented): The method according to claim 21 wherein the first solvent and the second solvent are the same.

Claim 30 (previously presented): The method according to claim 21 wherein the first solute is selected from the group consisting of biologically active materials, medicinal agents, sugars, pigments, toxins, insecticides, viral materials, diagnostic aids, agricultural chemicals, nutritional materials, proteins, alkyloids, alkaloids, peptides, animal and/or plant extracts, dyes, explosives, paints, polymer precursors, cosmetics, antigens, enzymes, catalysts, nucleic acids, and combinations thereof.

Claim 31 (previously presented): The method according to claim 21 wherein the supercritical fluid is carbon dioxide.

Claim 32 (previously presented): The method according to claim 21 wherein the first solution comprises an emulsion.

Claim 33 (previously presented): The method according to claim 21 wherein the first solution comprises a suspension of the first solute in the form of solid phase particles dispersed in the first solvent.

Claim 34 (previously presented): The method according to claim 21 wherein a polymer, lipid and/or excipient is dissolved in the second solvent, and wherein the precipitated particles collected in the collecting step comprise have a core comprising the first solute and a shell comprising the polymer, lipid and/or excipient.

Claim 35 (previously presented): The method according to claim 21 wherein the particles collected in the collecting step are substantially uniform and have an average diameter of less than about 5 μm.

Claim 36 (previously presented): The method according to claim 21 further comprising the step of:

adjusting the rotational speed of the rotor, the size of the space between the inner surface of the chamber and the adjacent surface of the rotor, and/or the flow rate of the supercritical fluid, the first solution and/or the second solution into the chamber to obtain precipitated particles having a desired average particle size.

Claim 37 (previously presented): Particles formed according to the method of claim 21.